## REMARKS

Applicant wishes to thank Examiner Navarro for the courtesy extended to Nancy Vensko, attorney of record, on July 21, 2005. The Interview Summary Form PTOL-413 summarizes the discussion held at the personal interview. The present response to the outstanding Office Action includes the substance of the Examiner Interview.

A. Disposition of Claims

Claims 5-12 are pending in this application. Per Office Action dated 11 Feb 2005 at p. 2, ¶¶ 1-2, Claims 13-16 have been canceled without prejudice as being drawn to non-elected subject matter. Claims 1-4 have been canceled without prejudice, and Claims 5-8 and 11 have been amended to more specifically describe the claimed subject matter and thus for reasons unrelated to patentability. Support for the amendment is found throughout the patent specification, for example, in the originally filed claims and at p. 7, line 23 – p. 8, line 21. Additionally, the incorporation-by-reference statement in the benefit claim has been deleted because this application represents the U.S. national phase of an international application and claims the benefit of priority of a U.S. provisional application, thus the incorporation-by-reference statement is redundant. No new matter has been added. Reexamination and reconsideration of the application, as amended, are respectfully requested.

B. Compliance with 35 USC 112/1 enablement

The issue is whether Claims 7-10 are in compliance with 35 USC 112, first paragraph, as meeting the enablement requirement. The Patent Office takes the position that the specification, while being enabling for antibodies that bind EBA-175, does not provide enablement for antibodies that inhibit *P. falciparum* invasion into a red blood cell *in vivo*. The test for enablement under MPEP 2164.01 is whether the application, when filed, contains sufficient information regarding the subject matter of the claims as to enable one skilled in the pertinent art to make and use the claimed invention. Example 2 describes MAb R256, which is an antibody that specifically binds a region of a RII/F2 region of an EBA-175 protein from a *Plasmodium* species, where the region consists of a 10 amino acid sequence and where the amino acid sequence is shown in SEQ ID NO: 1. Beginning with Claim 7, which requires that the antibody inhibit binding of an EBA-175 protein to a red blood

cell, Example 2 demonstrates that representative MAb R256 blocks the binding of EBA-175 to erythrocytes. Turning to Claim 8, which requires that the antibody inhibit *Plasmodium falciparum* invasion into a red blood cell, and Claim 9, which requires that the antibody inhibit *Plasmodium falciparum* invasion of a red blood cell *in vitro*, Example 2 establishes that representative MAb R256 inhibits merozoite invasion of erythrocytes *in vitro*. R256 blocked merozoite invasion in the homologous FVO strain. Additionally, R256 blocked merozoite invasion in the heterologous 3D7 strain. Ending with Claim 8, described above, and Claim 10, which requires that the antibody inhibit *Plasmodium falciparum* invasion of a red blood cell *in vivo*, invasion of merozoites into erythrocytes is dependent on the successful binding of parasite ligands to erythrocyte receptors. Thus inhibition of invasion would be a direct consequence of a blocking of binding of EBA-175 to erythrocytes. Similar to blocking of binding of EBA-175 to erythrocytes by R256, R256 inhibited merozoite invasion *in vitro*. Likewise, similar to blocking of EBA-175 to erythrocytes by R256, R256 should inhibit merozoite invasion *in vivo*. In accord with this prediction, the post-filing date art of Jones et al., 2001, J Infect Dis 183: 303, attached, (co-authored by the inventors) demonstrates that immunization with EBA-175 region II induces a significant antiparasite effect *in vivo*.

Ohas et al., 2004, Infect. Immun. 72: 735 is not contradictory. Ohas 2004 determined whether naturally acquired antibodies have a functional role by inhibiting binding of RII of EBA-175 to erythrocytes. There is no reason to equate antibodies against the parasite with antibodies against SEQ ID NO: 1. Attached is Purcell RH. Hepatitis E: prospects for immunoprophylaxis. In Margolis HS, Alter MJ, Liang TJ, Dienstag JL, eds. *Viral Hepatitis and Liver Disease. Proceedings of the 10th International Symposium on Viral Hepatitis and Liver Disease* 2000. Atlanta, International Medical Press, Ltd. 2002:97-102. In the paragraph bridging p. 98 and 99, the author explains how truncations of HEV ORF-2 have superseded the full-length protein because of unexpected properties of ability to fold into native configurations that reveal bona fide neutralization sites. By analogy, here, truncations of the full-length EBA-175 protein might reveal important neutralization sites masked by the parasite. Thus, while antibodies against the parasite may not play a role in conferring immunity to clinical malaria, Ohas 2004 does not contradict the role of antibodies against SEQ ID NO: 1 in providing protection as a vaccine. Moreover, Jones 2001 is in accord with this prediction. The conclusion is that the claims are in compliance with 35

USC 112, first paragraph, as meeting the enablement requirement.

C. Compliance with 35 USC 112/2

The issue is whether the claims are in compliance with 35 USC §112, second paragraph, as being definite. The phrase "cysteine rich region" was deleted as being drawn to superfluous subject matter. The conclusion is that the claims are in compliance with 35 USC §112, second paragraph, as being definite.

D. Compliance with 35 USC 102(b)

The issue is whether the claims are in compliance with 35 USC 102(b) or anticipated by WO 96/40766 to Sim et al. The rule according to MPEP 2131 is that to anticipate a claim, the reference must teach every element of the claim. WO 96/40766 describes the over 300 amino acid RII/F2 region of the EBA-175 protein. The subject matter of the claims is distinguished therefrom by selecting the 10 amino acid sequence of SEQ ID NO: 1 from the over 300 amino acid RII/F2 region of the EBA-175 protein for producing an antibody that inhibits merozoite invasion of RBCs and blocks binding of EBA-175 to erythrocytes. It was already known that the over 300 amino acid RII/F2 region of the EBA-175 protein was responsible for mediating binding to erythrocytes. Nevertheless, it was nowhere taught in the prior art that antibodies raised against the particular sequence of SEQ ID NO: 1 would result in the inhibition of merozoite invasion of RBCs and blockade of binding of EBA-175 to erythrocytes. Thus, the selection of said 10 amino acids for raising antibodies resulted in an unexpected and surprising effect. Consequently, the subject matter of the claims is novel and nonobvious. The conclusion is that the reference fails to anticipate the claims, thus the claims are in compliance with 35 USC 102(b).

## CONCLUSION

In view of the above, it is submitted that the claims are in condition for allowance. Reconsideration and withdrawal of all outstanding rejections are respectfully requested. Allowance of the claims at an early date is solicited. If any points remain that can be resolved by telephone, the Examiner is invited to contact the undersigned at the below-given telephone number.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

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By: _____

Nancy W. Vensko
Registration No. 36,298
Attorney of Record
Customer No. 45,311
(805) 547-5580

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